VARIABILITY OF THE RELATIVE CORPUS CALLOSUM CROSS SECTIONAL AREA BETWEEN DYSLEXIC AND NORMALLY DEVELOPED BRAINS

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ABSTRACT

Minicolumnar disturbance is a common feature to both dyslexic and autistic brains. This paper is motivated by the persistent need to investigate the effect of minicolumnar disturbance on the magnetic resonance images of the brain. This will serve as a preliminary step to develop a non-invasive methodology to discriminate between the diseases based on the MRI findings.
In this paper, we investigate the variability of the ratio between the corpus callosum cross sectional area and the total brain intracranial volume between two groups; a group of dyslexic patients and another group of normal controls. The results show that this ratio differs significantly between the two groups and that it can be used as a discriminatory feature between dyslexic brains and typically developed ones.

Index Terms: Brain, Magnetic Resonance Imaging, Dyslexia.

1. INTRODUCTION

Minicolumns are vertical organizations of neurons with similar functional properties and anatomical connections [1]. The most highly respected neurobiology textbooks consider the minicolumn, rather than a single neuron, as the basic unit of the brain cortex. We believe that any disturbance in the structure, number or organization of these minicolumns will have an immediate impact on the development of the brain, and hence its functionality [2].
In [2], we have started a project to investigate the impact of the pathological findings, in terms of the number and widths of minicolumns reported in [3], on the magnetic resonance imaging of the dyslexic brains. The major goal of the project is to find a collection of features from the MRI that serve as a signature of the dyslexic brain and help developing a non invasive computer aided diagnosis system that has the ability to differentiate between the dyslexic and typically developed brains through the MRI findings. In this paper, we study the effect of the minicolumnar disturbance on the ratio between the midsagittal callosal area and the total brain intracranial volume.
The rest of the paper is organized as follows: Section 2 will introduce the motivation to our work, justify our choice to this feature in particular and present the description of the data set. Section 3 will present the methodologies used for skull stripping, segmentation, corpus callosum extraction and the hypothesis that we propose to test. Sections 4 and 5 will introduce the experimental results and conclusions, respectively.

2. PROBLEM STATEMENT AND DATA SET DESCRIPTION

Dyslexia and autism are two of the most complicated brain developmental disorders that affect the learning abilities in children. One of the major causes of developmental disorders is that some parts of the communications network of the brain fails to perform its tasks properly. The failure to develop proper communications between the different brain parts can be caused by the disturbance in the brain minicolumnar structures. Meanwhile, the disturbance of the number and widths of the minicolumns is proved to be a common feature to both dyslexia autism [3, 2]. Dyslexia and autism are found to be in opposite tails of the minicolumnar width distribution. Patients with autism tend to have lager number of minicolumns that have smaller width than the normal. On the other hand, dyslexia is on the opposite tail, having smaller number of minicolumns. The decreased number of minicolumns in dyslexia is expected to have an impact on the communication between the two hemispheres. We expect a reduction in the intrahemispheric connections through the minicolumnar structures and an increased interhemispheric connectivity through the corpus callosum. In other words, we hypothesize that the disturbance in the number of minicolumns will cause an increase in the number of commissural fibers traversing the corpus callosum. To our knowledge, there is no estimate for the number of these fibers in dyslexic or autistic brains. So, we propose to study the cross sectional area of the corpus callosum in the midsagittal section. This area reflects the number of of commissural fibers crossing the corpus callosum. But, since there is an evidence of a significance difference between the brain volumes of the dyslexic and normal brains [2], using the absolute area is misleading and may not reflect the real difference between the two groups. The difference may diminish or become more dominant if the volume differences are taken into consideration. Hence, we will analyze the significance of the difference of the ratio between the cross sectional area of the corpus callosum and the total brain volume between dyslexic brains and typically developed ones, rather than the absolute areas. On another hand, several studies in autism have shown a reduction in the cross sectional area of the corpus callosum [4]. The duality of pathological findings in dyslexia and autism suggests duality in MRI findings as well. Hence, our hypothesis of having an increased corpus callosum cross sectional area in dyslexia should be a valid

hypothesis. Up to date, there has been a lot of conflicting evidence regarding the development, size and shape of the corpus callosum in developmental dyslexia. For a review of several MRI studies regarding this matter we refer the reader to [5]. *However, we would like to emphasize that our paper here is not intended to increase the conflict by one but to present another perspective to the analysis of the corpus callosum variability through the minicolumnar hypothesis. In other words, the paper is intended to introduce the correlation between the pathological findings expressed by the disturbance of the number and width of minicolumns [3] and the MRI findings expressed in the ratio between the midsagittal callosal area and the total brain volume. From another perspective, the paper presents an evidence from the MRI that supports the minicolumnar hypothesis [6] and the duality of findings between dyslexia and autism.*

2.1. Data Set and MRI Protocol

The data set consists of twelve right handed dyslexic men aged 18 to 40 years, and a group of twelve controls matched for gender, age, educational level, socioeconomic background, handedness, and general intelligence. All the subjects are physically healthy and free of history of neurological diseases, or head injury. Briefly, all the subjects have exactly the same psychiatric conditions. All images were acquired with the same 1.5 T MRI scanner (GE, Milwaukee, Wisconsin) using a 3-D spoiled gradient recall acquisition in the steady state (time to echo, 5 milliseconds; time to repeat, 24 milliseconds; flip angle, 45; repetition,1; field of view, 24 cm^2). Contiguous axial slices, 1.5 mm thickness (124 per brain) were obtained and the voxel resolution was 0.9375*0.9375*1.5mm.

3. METHODS

The proposed approach consists mainly of four steps; first, a skull stripping is applied to all the volumes to remove all the non brain tissue. Second, brain segmentation is performed to extract the white matter. Third, the midsagittal slice is calculated and a connected components analysis is performed on the white matter of the midsagittal slice to isolate the corpus callosum. Finally, volumes and areas are calculated and tests of hypothesis are performed to investigate whether there is a significant difference between the different groups or not. The following subsections will give a brief description of each of the aforementioned steps.

3.1. Brain extraction and segmentation

The MRIcro[1] has been used for skull stripping to extract the brain. Then a hierarchical model that incorporates active contours for front propagation and graph cuts for optimization is used to segment the white matter. The segmentation problem is described as follows:

- Input: the input is an image $u(x, y)$ consisting of three regions ω_1, ω_2 and $\omega_3 \subset \Omega$. The mean intensity values in these regions are m_1, m_2 and m_3, respectively.WLOG, assume that $|m_2 - m_1| < |m_3 - m_2|$ and $|m_1 - m_3|$
- Objective: The objective is to obtain a labeling $L = [l_1\ l_2\ l_3]$ such that

$$L(x,y) = \begin{cases} l_1, & \text{if } (x,y) \in \omega_1, \\ l_2, & \text{if } (x,y) \in \omega_2, \\ l_3, & \text{Otherwise.} \end{cases} \quad (1)$$

We have solved the segmentation problem in a sequential manner by classifying the input image into two regions $R_1 = \omega_1 \bigcup \omega_2$ and $R_2 = \omega_3$, then the next step of the segmentation algorithm classifies R_1 into ω_1 and ω_2. This is done by minimizing the energy function

$$\begin{aligned} E &= \lambda_1 \sum_p (u_p - c_1)^2 x_p + \lambda_2 \sum_p (u_p - c_2)^2 (1 - x_p) \\ &+ \mu \sum_{p,q \in e_k} w_k (x_p(1 - x_q) + x_q(1 - x_p)) \end{aligned} \quad (2)$$

where λ_1, λ_2 and μ are constants that reflect the effect of each of the energy terms (Throughout this paper we used $\lambda_1 = \lambda_2 = 1$ and $\mu = 0.1 \times 255^2$), u_p is the intensity level of the pixel $p = (x, y)$ and x_p is a binary variable that is equal to 1 inside R_1 and zero, otherwise.The third term is just a discrete representation of the length of the evolving front that separates the two different classes, e_k is the edge connecting vertices v_p and v_q (corresponding to two neighboring pixels in the image), and w_k is the capacity of the edge e_k. c_1 and c_2 are the mean intensity values in R_1 and R_2, respectively and updated after each curve evolution step using the following equations;

$$c_1 = \frac{\sum_p u_p x_p}{\sum_p x_p}, \text{ and } c_2 = \frac{\sum_p u_p (1 - x_p)}{\sum_p (1 - x_p)}. \quad (3)$$

The energy function E is minimized iteratively using graph cuts. After each iteration, the min cut is calculated. The values of the binary variable x_p are updated according to the min cut, and accordingly, the values of c_1 and c_2. The iterations are terminated when the energy is minimized and c_1 and c_2 become fixed. The final values of x_p represent the pixel labeling. The same scenario is repeated to isolate ω_1 and ω_2. For further details about the graph construction, computational complexity, quantitative results of the segmentation approach and comparison to other existing segmentation techniques, we refer the reader to [7, 8]. However, we would like to point out that our segmentation results were more balanced than other standard approaches (SPM, FSL)[2] which led to better white matter segmentation. This reflects on the accuracy of the corpus callosum extraction and hence we expect our results and measurements to be more robust than most of the previously published studies that analyze the corpus callosum differences among different individuals.

[1] MRIcro is available at http://www.sph.sc.edu/comd/rorden/mricro.html

[2] Quantitative comparison was provided in [8]

3.2. Extraction of the corpus callosum and hypothesis tests

After segmenting the white matter, the segmented white matter midsagittal slice will have two dominant components; the corpus callosum and the brain stem. We applied connected component analysis to extract the corpus callosum based on a predefined statistical model that suggests that the corpus callosum is the second dominant component in the midsagittal slice.
Having extracted the corpus callosum, the statistical analysis consists of the following steps;

1. The total brain volume (TBV) of each individual has been calculated. The means (μ_{TBV_N} and μ_{TBV_D}) and standard deviations (σ_{TBV_N} and σ_{TBV_D}) for normals and dyslexic, respectively, were calculated.

2. The cross sectional area of the corpus callosum (CCA) has been calculated for all the cases. The means (μ_{CCA_N} and μ_{CCA_D}) and standard deviations (σ_{CCA_N} and σ_{CCA_D}) for normals and dyslexic, respectively, were calculated.

3. The ratio between the corpus callosum cross sectional area and the total brain volume for each case has been calculated. The mean and standard deviation of the ratio for the control cases, μ_{R_N} and σ_{R_N}, respectively were calculated. The corresponding mean and standard deviation for the dyslexic group, μ_{R_D} and σ_{R_D}, were calculated as well.

4. Two main hypothesis tests are performed: A test to decide whether the samples (of the calculated ratios) came from a normal distribution or not. Another hypothesis test with the null hypothesis μ_{R_N}=μ_{R_D} is performed to test whether or not there is a significant difference of the corpus callosum cross sectional area relative to the total brain size between the dyslexic patients and the normal control cases and then in case of finding a significant difference, we will perform a one tailed test on the mean values.

4. EXPERIMENTAL RESULTS

This section shows sample results of our segmentation to the white matter and extraction of the corpus callosum. It will also include the measurements that we have obtained for the data set and the results of the hypothesis testing.

4.1. Corpus callosum extraction and measurements

Figure 1 shows the subsequent steps of extracting the corpus callosum. At the first step, the active contour is initialized as a circle in the middle of the image and is allowed to deform according to the energy function introduced in Section 3. The final evolution results in a contour that isolates the cerebrospinal fluid in the first class and groups the white matter and gray matter in the second class. Consequently, the second class has a higher intensity variation and hence is passed to the next segmentation step in which the white matter and gray matter are separated in different classes. In figure 1(e), we show the segmented white matter tissue. Then (f) and (g) show the connected components of the white matter and the corresponding frequency histogram, respectively. The histogram shows that the component labeled 9 has the second highest frequency and hence identified as the corpus callosum and the segmented corpus callosum is shown in (h).

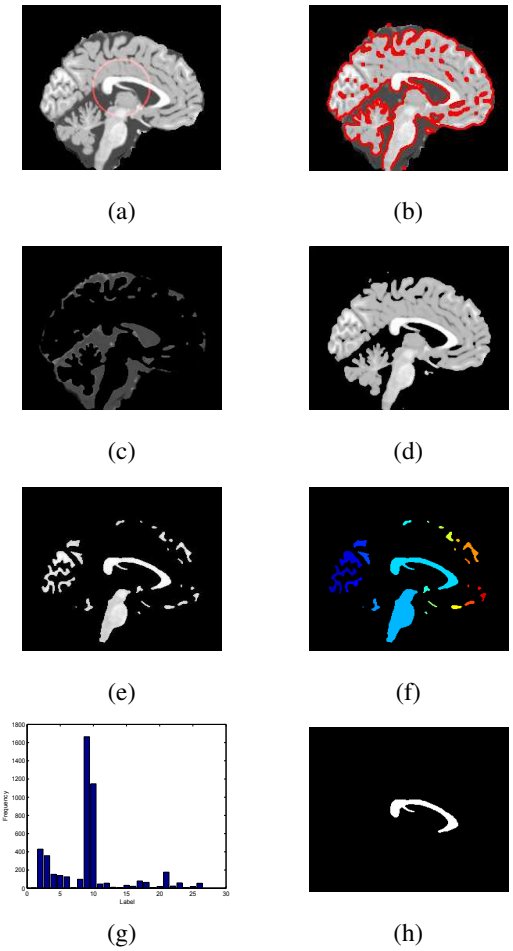

Fig. 1. Extraction of the corpus callosum in the midsagittal slice. (a) The skull stripped MRI slice initialized by a contour C:$\sqrt{(x-128)^2+(y-90)^2}-40$, (b) the contour after the first step of the evolution, (c) the CSF separated in one class, (d) the WM and GM grouped in one class that will be passed to the next segmentation step to separate each tissue, (e) The segmented WM, (f) the connected components of the segmented white matter, (g) the frequency histogram of the connected components and (h) the extracted corpus callosum corresponding to component that has the second highest frequency.

Table 1 shows our measurements for the midsagittal callosal area, the total brain volume and the ratio between them for the normal control cases. Table 2 shows the corresponding measurements for the dyslexic group.

4.2. Results of the hypothesis tests

The Lilliefors goodness of fit test has been applied to the ratio values for normal control sample as well as the dyslexic sample.

Table 1. Measurements of the corpus callosum cross sectional area (CCA), the total brain volume (TBV) and the ratio between them for 12 normal controls.

Case Number	CCA cm^2	TBV cm^3	R=$\frac{CCA}{TBV}$ $\times 1000\ cm^{-1}$
1	6.9047	1710.8	4.0359
2	7.3828	1489.7	4.9559
3	7.2281	1553.4	4.6531
4	7.2281	1494.6	4.8361
5	7.425	1583.7	4.6884
6	6.6094	1277.9	5.1721
7	6.5672	1598	4.1096
8	8.255	1537.1	5.3705
9	7.762	1641	4.73
10	9.323	1640.9	5.6816
11	7.664	1626.9	4.7108
12	7.144	1372.9	5.2036
Mean	7.4578	1543.9	4.8456
Std	0.7555	121.95	0.4779

Table 2. Measurements of the corpus callosum cross sectional area (CCA), the brain volume (TBV) and the ratio between them for 12 dyslexic patients.

Case Number	CCA cm^2	TBV cm^3	R=$\frac{CCA}{TBV}$ $\times 1000\ cm^{-1}$
1	7.3969	1448.6	5.1062
2	7.20	1391.3	5.175
3	6.525	1550.2	4.2091
4	7.5656	1391.2	5.4382
5	7.2984	1507.3	4.842
6	7.5375	1438	5.2417
7	7.2703	1456.5	4.9916
8	8.269	1397.3	5.9178
9	8.114	1546.8	5.2457
10	9.464	1462.9	6.4693
11	8.128	1406.8	5.7777
12	9.422	1471.9	6.4013
Mean	7.8492	1455.7	5.4013
Std	0.8843	56.14	0.6495

The test was used to determine whether the considered samples came from a normal distribution or not. We tested the null hypothesis that the samples came from a normal distribution at a confidence level $\alpha = 0.05$, the null hypothesis has been accepted for both samples and hence we can apply the Student's t-test to examine the difference of the means between the two different groups.

The Student's t-test has been applied to test the null hypothesis that $\mu_{R_N} = \mu_{R_D}$. The test was performed using a confidence level $\alpha = 0.05$ and resulted in rejecting the null hypothesis that the there is no significant difference between the means of the ratio of the dyslexic sample and the normal sample and accepting the alternative hypothesis that suggests that there is a significance difference. We also tested the null hypothesis that $\mu_{R_D} > \mu_{R_N}$ at two confidence levels $\alpha = 0.05$ and $\alpha = 0.01$. The null hypothesis was accepted in both cases. Hence, the results of the the hypothesis testing suggest that the ratio of the relative corpus callosum size of dyslexic brains is significantly larger than its corresponding in typically developed brains.

5. CONCLUSION AND FUTURE WORK

The paper investigated the difference between the ratio of the midsagittal callosal area and the total brain volumes in dyslexic patients versus normal control cases. The segmentation of the white matter hierarchical graph cut based active contour that guarantees global optimization of the contour energy. The corpus callosum is extracted from the white matter segmented midsagittal slice using connected component analysis. The ratio has been calculated for both samples; the normal and dyslexic. The results of the hypothesis tests suggest that the ratio of the cross sectional area of corpus callosum to the brain brain volume in dyslexic brains is significantly larger than its corresponding values in normally developed brains. This ratio actually reflects the number of commissural fibers crossing the corpus callosum. Hence, the functional implications of our result is that dyslexic brain tend to prefer interhemispheric connections through the corpus callosum over the intrahemispheric connections through the minicolumns in the neocortex. Thus it correlates with the smaller number of minicolumns in dyslexic brains. This ratio can be used as one discriminatory feature between dyslexic and non dyslexic brains from MRI. For future work, we are planning to investigate more features to build a unique signature that may help to build a computer aided diagnosis system for dyslexic brains.

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